EARLY ARTHRITIS ASSOCIATED WITH CROHN’S DISEASE – A DIAGNOSTIC CHALLENGE. SOME CONSIDERATIONS ON A CLINICAL CASE

LIANA CHICEA1, LAURA DAMIAN2, SIMONA GRAD3

1“Lucian Blaga” University of Sibiu, Clinical County Emergency Hospital Sibiu, 2Rheumatology Clinic Cluj-Napoca, 3II Medical Clinic Cluj-Napoca

Keywords: Crohn’s disease, seronegative spondyloarthritides pseudotumoral

Abstract: This is a case report of a male patient with peripheral seronegative spondyloarthritides associated with pseudotumoral Crohn’s disease. Difficult diagnosis and therapy problems occurred at the disease onset, shortly after the surgery for haemorrhagic duodenal ulcer and together with an abdominal pericolonic mass. We reviewed the literature data on these particular issues.

Cuvinte cheie: boala Crohn, spondilartrită seronegativă, pseudotumoral

Rezumat: Prezentăm cazul unui pacient cu spondilartrită seronegativă perițierică asociată cu boală Crohn. La debutul afecțiunii articulare, simulat cu o formăție pericolonică și ulcer duodenal hemoragic, problemele de diagnostic și tratament au fost complexe. Am reluat câteva discuții din literatura de dată recentă pe marginea acestui caz,

INTRODUCTION

This is the clinical case of a male patient presenting with recent onset polyarthritis which occurred and developed in clinical particular circumstances. Its diagnosis and treatment raised difficult problems and required a multidisciplinary approach.

CASE REPORT

G.L., 44 years old, male, was admitted in the Emergency Room for upper gastrointestinal haemorrhage (UGIH) and secondary severe anemia (Hb – 7.6 g/dl, most probably occurred after occult previous gastrointestinal bleeding). He used some NSAIDs for mechanical chronic low back pain that gradually increased during last year and that was diagnosed (MRI) as multiple lumbar disk and spine degenerative disease with radiculopathy L3-S1. Endoscopy performed in the Emergency Room revealed large duodenal ulcer with an adherent clot, so immediate treatment consisting in naso-gastric tube placement, local wash-out and intravenous (IV) haemostatics and proton pump inhibitors were initiated. The next few days showed minimal improvement and in the 7th day, massive bleeding repeated and haemorrhagic shock was also diagnosed. Surgery was performed and duodenal ulcer penetrating haepatic vessels with vascular bleeding fistulae was cured by piloroplasty, bilateral troncular vagotomy and multiple peritoneal drainage, followed by slow surgical recovery.

Ten days after surgery, rheumatologic examination was required for gradual onset polyarthralgias with both axial and peripheral distribution, large and small afflicted joints (knees, ankles, shoulders, proximal interphalangeal and metatarsal phalangeal joints in hands). First diagnosis was recent onset arthritides, and early rheumatoid arthritis or seronegative spondiloarthritides onset were considered so, that supplementary lab tests (erythrocyte sedimentation rate, C reactive protein, rheumatoid factor, anti-CCP antibodies and hands radiography) and anti-inflammatory (Paracetamol, Celecoxib protected with Pantoprazole), intraoperative lead substitution and antialgic treatment (Tramadol) were recommended for the next 5-7 days.

The patient leaved the hospital but came back after two weeks for increased disabling inflammatory multiple joint pain and 10 kg weight loss during the last month. Physic exam revealed generalized oedema with hypoproteinotic pattern (total serum proteins = 5.6 mg/dl), pale skin, swollen (2) and tender (8) joints with soft tissue oedema and rheumatoid pattern while serum proteins = 5,6 mg/dl, FR neg, ACPA neg, C3=VN, AAN=neg) inflammation (ESR repeatedly higher than 100 mm/1h, CRP =364 mg/dl, FR neg, ACPA neg, C3=VN, AAN=neg)

Joints Rx examinations (hands and adiocarpal joints, knees, coxofemoral, sacroiliac joints) were normal.

Work-up continued for gut involvement, mainly for suspected inflammatory intestinal disease (Crohn’s disease suspected the most, since no recto/sygmoidal involvement clinically evidenced) and possible neoplastic disease as well. Abdominal ultrasound had no diagnostic findings (except liver steatofibrosis). Endoscopy revealed no bleeding but persistent gastric and duodenal inflammatory non-specific findings. Colonoscopy ruled out the inflammatory intestinal disease. Abdominal CT showed a mass surrounding the ceccum and Colonoscopy ruled out inflammatory intestinal disease. Colonoscopy ruled out the inflammatory intestinal disease.

Laparoscopy was not recommended by surgeons. With no biopsy, differential diagnosis included intestinal tuberculosis (most frequently localised at the intestinal-bowel junction, general signs of infection, but no specific signs such as positive
Quantiferon or tuberculin skin test (that was not performed due to financial reasons), intestinal abscess consecutive to previous surgery, pseudotumoral Crohn’s disease (low incidence, no previous suggestive signs, no specific endoscopic diagnosis), abdominal mass (confirmed at CT but unspecific; abdominal MRI postponed).

Some modifications described were cholestasis and transient hepatocytolysis, consequent to ulcerous disease, and also suggestive for Hyper-Ig G4 syndrome (cholangitis + pericolonic mass).

The patient underwent an antibiotic treatment associated withcox-2 selective anti-inflammatory drugs, amino acids, other symptomatic drugs, and he had a good outcome. Nevertheless, the abdominal mass persisted for longer than a month with no signs at repeated endoscopic and CT investigations.

Investigations have been resumed and continued in other service. One month after initiating Sulfasalazine, the rheumatoid syndrome was significantly improved and the laboratory tests showed hyperuricemia (10.4 mg/dl), GGT isolately increased (69 U/L), mild macroctic anemia (Hb=11.8 mg/dl), mild inflammation (VHS=30 mm/ 1h). Further enquiries carried out have investigated probable diagnoses such as gut tumour (19-9 Antibody=normal value NV), autoimmune cholangitis (Anti-p-ANCA=neg), hyper IG G4 syndrome (IG G4 =NV), intestinal inflammation (increased Calprotectin). Abdominal ultrasound had no pathological changes, except minimum proximal bowel parietal thickening (7mm) and distension. However, colonoscopy resumed showed distal ileitis (without tumour) with histological aspect of intestinal reactive inflammation that suggested Crohn’s disease. Treatment with Sulfasalazine was continued, since it is the most appropriate medication for seronegative spondylarthitis associated with inflammatory diseases. In another two months, Colchicine was added (persistent hyperuricemia), with good outcome considering both joints and general, so that after 6 months the patient has returned to the weight he had previous suggestive signs, no specific endoscopic diagnosis), abdominal mass (confirmed at CT but unspecific; abdominal MRI postponed).

In this clinical case, we experienced some problems in the diagnostic interpretation on:
1. Joints complaints, early arthritis/ undifferentiated arthritis respectively. At the beginning, the type and distribution of pain were mixed (mechanical and inflammatory type, axial and peripheral joints, large and small joints, upper land lower limbs). Most often we consider rheumatoid arthritis (but no criteria were met for diagnosis at that time), or undifferentiated peripheral spondylarthritus, or arthritis with crystals (seldom having generalised manifestations), and infectious arthritis as well (least likely to a patient with no fever or other infection signs). Peripheral arthritis associated with intestinal inflammatory diseases, more frequently with Crohn’s disease is the most common extraintestinal manifestations of these diseases. We considered this diagnosis to be the most probable for our patient: the erosive, symmetric, small and large joints polyarthritis, with a natural course independent of the intestinal course, sometimes with associated uveitis (absent in this case) and HLA B44 antigen presence (not determined in our patient due to financial reasons). Current criteria for diagnosis of both seronegative spondylarthropathy and rheumatoid arthritis have not been quite useful in this case for the right early diagnosis.
2. Potential connection between upper digestive hemorrhage and inflammatory intestinal disease – is it a simple coincidence? Could it be the case of Crohn’s disease with gastro-duodenal fistulae the start of clinical manifestations and complications (hemorrhage, covered perforation and tumour mimic)? Is the abdominal mass described at CT a complication of the intestinal inflammatory disease? Or could it be a complication of the peptic disease?
3. How did arthritis start: does it have anything to do with surgery or there is a simple coincidence? Is arthritis revealing the presence of Crohn’s disease or of a proliferative neoplastic disease? In this context (hipoproteinemia and generalized oedema) clinical evaluation is difficult and misleading; using ultrasound evaluation of synovitis could have been more useful and more sensitive, providing data about enthesitis as well and giving guidance for a local treatment if needed?
4. Difficulty to prove the diagnosis of Crohn’s disease in the absence of elements of certainty (by histopathology, before it was performed).

Treatment was another challenge in this case. The remissive treatment should have been started as soon as possible, but it has been delayed - without exceeding the therapeutic window of opportunity - due to the massive bleeding and also to the suspected infection or neoplasia. The symptomatic therapy of pain (with non-steroidal anti-inflammatory drugs) in this context has raised safety issues.

DISCUSSIONS

Face to these diagnostics challenges, we searched the literature for the Hyper Ig G4 syndrome and Crohn’s disease.

Thus, the pseudotumoral Crohn’s disease is very rare as a presentation of the onset, with a prevalence of 2% (1), without specific symptoms and even without endoscopic diagnostic signs in more than a half of the cases with histological confirmation. Current criteria for diagnosis of Crohn’s disease (2).

Although characteristic muscularoskeletal clinical signs of seronegative spondylarthritus are often present in patients with intestinal inflammatory diseases, many people are not examined by a rheumatologist, so that gastroenterologists have a key role in early guidance of these patients with potentially invalidating disease.(3)

A significant percentage of patients with intestinal inflammatory diseases do not have clinical signs of spondylarthritus but have some other changes comparable to those of patients with spondylarthritus, such as enthesisitis, that can be diagnosed easily, early and accurately with an ultrasound examination.(4)

Whereas clinical symptoms are weakly correlated with inflammatory activity of Crohn’s disease, an attempt is made to find specific biomarkers and diagnostic tools in order to facilitate an accurate and early diagnosis. Combination of faecal calprotectin, MMP9 (matrix-metalo-proteinaze) and IL22 has the strong association with imaging (CT enterography) or endoscopic ileocolonoscopy degree of inflammation in Crohn's disease. (5)

Among next generation diagnostic methods for Crohn’s disease, enterography-MRI is useful for diagnosis, expansion, activity, complications of the disease, the response to treatment and careful decision making.(5) Ultrasonography use is advised also, mainly for selecting the patients for MRI.(6) Device-assisted enteroscopy, small-bowel capsule endoscopy, dye-based chromoendoscopy, magnification chromoendoscopy, dye-less chromoendoscopy, endoscopy and other special methods, such as Narrow band imaging and i-scan, Confocal laser endomicroscopy CLE, CLE-based molecular imaging, are currently developed and promising.(7)

For the histological diagnosis of the biopsies in...
intestinal inflammatory diseases. British Society of Gastroenterology has updated by the end of 2013 a guide to optimizing quality and consistency in the reporting of the results, which should be linked with clinical and endoscopic features and summarised in the acronym PAID (Pattern, Activity, Interpretation, Dysplasia).(9)

Hyper IgG4 syndrome, having many names which reflect symptoms, is characterized by lympho-plasmocytic infiltration of the tissues (predominantly IgG4 plasmocyte cells and T lymphocytes), frequently accompanied by fibrosis, fibroblasts obliteratora, and increased serum levels of the IgG4 in many patients. The disease has a good answer to corticotherapy, especially in its prefibrotic phase.(10,11,12) It has 4 types, namely type I - Multicentric Castleman disease-like, type II – follicular hyperplasia, type III – interfollicular expansion, type IV - progressive germinal centre transformation, type V – pseudotumoral nodal inflammation. It is more frequent in mean age men. Pathogenetic mechanisms are autoimmunity and allergic or paraneoplastic. A specific feature of the disease is the presence of pseudotumoral masses and adenopathies in different sites, sometimes mimicking specific conditions such as autoimmune pancreatitis, sclerosing cholangitis, Miculicz disease and sclerosing syaladenitis (tumour Kuttner), reticuloar inflammatory pseudotumour, inflammatory, chronic sclerosing dacryoadenitis, aortitis and chronic sclerosing periarteritis), pulmonary interstitial pneumonitis and pseudotumour, interstitial nephritis.

CONCLUSIONS

Crohn’s disease may have multiple organ manifestations, sometimes hard to be diagnosed. Associating them with spondiloarthritis can be misleading, as the pseudotumoral onset was in our patient. Early arthritis is often a challenging diagnosis, requiring a tight control. In some rheumatologic cases, early accurate diagnosis requires a multidisciplinary approach.

Acknowledgement:

To dr. Simona Grad (II Medical Clinic Cluj-Napoca), prof. dr. I. Sabău (I Surgery Clinic Sibiu) and dr. Laura Damian (Rheumatology Clinic Cluj-Napoca), who provided relevant data about the patient. Dr. Damian also assisted the writing of this paper.

REFERENCES